

Radiation Exposure Alters Expression of Metabolic Enzyme Genes In Mice

V. E. Wotring, Ph.D.¹, L.S. Mangala, Ph.D.², Y. Zhang, Ph.D.³ and H. Wu, Ph.D.⁴

¹Senior Scientist, JSC Pharmacology Discipline/Universities Space Research Association,

²University of Houston Clear Lake, ³Wyle Laboratories, Inc and ⁴NASA-Johnson Space Center
NASA, 2101 Nasa Rd 1, Houston TX 77058

INTRODUCTION

Most pharmaceuticals are metabolized by the liver. The health of the liver, especially the rate of its metabolic enzymes, determines the concentration of circulating drugs as well as the duration of their efficacy. Because of the importance of the liver in drug metabolism it is important to understand the effects of spaceflight on the enzymes of the liver. Exposure to cosmic radiation is one aspect of spaceflight that can be modeled in ground experiments. This study is an effort to examine the effects of adaptive mechanisms that may be triggered by early exposure to low radiation doses.

METHODS

Using procedures approved by the JSC Animal Care & Use Committee, C57 male mice were exposed to ¹³⁷Cs in groups: controls, low dose (50 mGy), high dose (6Gy) and a fourth group that received both radiation doses separated by 24 hours. Animals were anesthetized and sacrificed 4 hours after their last radiation exposure. Livers were removed immediately and flash-frozen in liquid nitrogen. Tissue was homogenized, RNA extracted and purified (Absolute RNA, Agilent). Quality of RNA samples was evaluated (Agilent Bioanalyzer 2100). Complementary DNA was prepared from high-quality RNA samples, and used to run RT-qPCR screening arrays for DNA Repair and Drug Metabolism (SuperArray, SABiosciences/Qiagen; BioRad Cfx96 qPCR System).

RESULTS

Of 91 drug metabolism genes examined, expression of 7 was altered by at least one treatment condition. Genes that had elevated expression include those that metabolize promethazine and steroids (4-8-fold), many that reduce oxidation products, and one that reduces heavy metal exposure (>200-fold). Of the 91 DNA repair and general metabolism genes examined, expression of 14 was altered by at least one treatment condition. These gene expression changes are likely homeostatic and could lead to development of new radioprotective countermeasures.